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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,645	07/23/2003	Claudio Pisano	4865-74	6903

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
01/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/624,645	PISANO ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-78,86-105 and 107-115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-78, 86-105 and 107-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 12-3-08 is acknowledged.

Claims included in the prosecution are 71-78, 86-105 and 107-115.

In view of the amendments, the rejection of claims over Hsu in view of Wang is withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 71-78, 86-105 and 107-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The negative limitation, "with the proviso that said liposome is not: miristoyl k-carnitine chloride tetradecyl ester. palmitoyl L-camitine bromide hexadecyl ester. oleyl L-carnitine chloride oleyl ester" now introduced in the independent claims has no support in the specification as originally filed and therefore, deemed to be new matter. The examiner suggests reciting specific compounds instead of the negative limitations.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 77-78, 86-105 and 107-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The independent claims now recite “consisting of” which is a closed expression and thus does not permit the addition of any other component in the liposomes. Claims 77-78 however, recite the presence of a helper lipid which is improper. Similar is the case with claims 91-92 and 100-101. It is also unclear as to what applicant intends to convey by ‘possible enantiomers’ and ‘relative admixtures’ in the independent claims.

The distinction between ‘sulfate’ and ‘acid sulfate’, 'citrate' and 'acid citrate', and similar expressions in claims 74, 89 and 97 is unclear.

The examiner suggests the deletion of ‘-' in “7-butoxyiminomethylcam-ptothecin’ (claims 76, 99).

Applicant selectively excludes certain carnitine derivatives in the independent claims. However, the dependent claims 75, 90, 98 recite the excluded compounds.

It is unclear as to what the limitation in parenthesis in claim 115 represents.

Claim Rejections - 35 USC § 103

5. . The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 71-78 and 86-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al in combination with Allen (6,056,973), Burke (5,552,156), in further combination with Stracher (5,008,288).

Wang et al disclose cationic liposome compositions containing claimed alky acyl carnitine esters for gene delivery. The fatty acid groups are oleyl or myristoyl, palmitoyl or stearoyl groups. The liposomes contain helper lipid (DOPC), cholesterol. The liposomes are administered intravenously (abstract, Scheme 1 on page 2208, Tables 3 and 4 on page 2211, page 2214, col. 2).

What is lacking in Wang et al is the teaching of the use of claimed drugs such as anti-cancer drugs, camptothecins in particular.

Allen teaches that liposomes are delivery agents for anticancer drugs such as camptothecin derivatives and genes (abstract, col. 16, lines 10-17).

Burke teaches that liposome stabilize camptothecin derivatives (abstract, examples and claims).

Stracher teaches that because of the presence of carnitine or its derivatives as part of liposomal structure, the drug containing liposomes will be delivered in much greater amounts to the desired target organs and much less is metabolized by the liver (abstract, col. 17, line 51 through col. 18, line 44). According to Stracher, carnitine derivatives by themselves can be used in the formation of liposomes without other phospholipids (Example 5).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Wang et al to delver drugs other than genes, such as anti-cancer drugs or cosmetic agents with a reasonable expectation of success since liposomes are known drug and cosmetic agent carriers and as evident from Allen, the term drug encompasses genes and anti-cancer agents such as camptothecin derivatives and liposomes are carriers for both genes and anti-cancer agents. One of ordinary skill in the art would use camptothecin derivatives as drugs since they are known to be encapsulated in liposomes because of stabilization by liposomes as taught by Burke. One of ordinary skill in the art would be motivated to use carnitine derivatives containing liposomes of Wang et al for the delivery of camptothecin derivatives of Burk since Stracher teaches the advantages of the presence of carnitine derivatives in liposomal structure in the drug delivery.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that instant amended claims exclude the compounds of Wang. This argument is not persuasive since the excluded compounds in the independent claims are still recited in the dependent claims. Furthermore, Wang teaches the applicability of several carnitine derivatives. Therefore, it is within the skill of the art use carnitine esters with suitable fatty acid chains with a reasonable expectation of success. Applicant's arguments that instant claim language excludes the helper lipid taught by Wang are not persuasive since the reference of Stracher clearly shows that one can form liposomes with just carnitine derivatives and applicant has not shown any unexpected results by excluding the lipids taught by Wang. .

7. Claims 71-78, 86-105 and 107-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al in combination with Allen (6,056,973), Burke (5,552,156), Stracher (5,008,288) and Szoka (5,811,406) of record.

Wang et al disclose cationic liposome compositions containing claimed alky acyl carnitine esters for gene delivery. The fatty acid groups are oleyl or myristoyl, palmitoyl or stearoyl groups. The liposomes contain helper lipid (DOPC), cholesterol. The liposomes are administered intravenously (abstract, Scheme 1 on page 2208, Tables 3 and 4 on page 2211, page 2214, col. 2).

What is lacking in Wang et al is the teaching of the use of claimed drugs such as anti-cancer drugs, camptothecins in particular. What is also lacking is the use of mannitol as the support material.

Allen teaches that liposomes are delivery agents for anticancer drugs such as camptothecin derivatives and genes (abstract, col. 16, lines 10-17).

Burke teaches that liposome stabilize camptothecin derivatives (abstract, examples and claims).

Stracher teaches that because of the presence of carnitine or its derivatives as part of liposomal structure, the drug containing liposomes will be delivered in much greater amounts to the desired target organs and much less is metabolized by the liver (abstract, col. 17, line 51 through col. 18, line 44). According to Stracher, carnitine derivatives by themselves can be used in the formation of liposomes without other phospholipids (Example 5).

Szoka discloses that formulations containing carnitine esters can be prepared in dry powder form using compounds such as mannitol (abstract, columns 9-11).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Wang et al to delver drugs other than genes, such as anti-cancer drugs or cosmetic agents with a reasonable expectation of success since liposomes are known drug and cosmetic agent carriers and as evident from Allen, the term drug encompasses genes and anti-cancer agents such as camptothecin derivatives and liposomes are carriers for both genes and anti-cancer agents. One of ordinary skill in the art would use camptothecin derivatives as drugs since they are known to be encapsulated in liposomes because of stabilization by liposomes as taught by Burke. One of ordinary skill in the art would be motivated to use carnitine derivatives containing liposomes of Wang et al for the delivery of camptothecin derivatives of Burk since Stracher teaches the advantages of the presence of carnitine derivatives in liposomal structure in the drug delivery. The use of compounds such as mannitol during the preparation of dry powders would have been obvious to one of ordinary skill in the art since the reference of Szoka shows that mannitol is a cryopreservative. Szoka also shows the use of carnitine esters by themselves.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore /
Primary Examiner, Art Unit 1612

GSK